

# CFGP 2.0: a versatile web-based platform for supporting comparative and evolutionary genomics of fungi and Oomycetes

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## ABSTRACT

In 2007, Comparative Fungal Genomics Platform (CFGP; <http://cfgp.snu.ac.kr/>) was publicly open with 65 genomes corresponding to 58 fungal and Oomycete species. The CFGP provided six bioinformatics tools, including a novel tool entitled BLASTMatrix that enables search homologous genes to queries in multiple species simultaneously. CFGP also introduced Favorite, a personalized virtual space for data storage and analysis with these six tools. Since 2007, CFGP has grown to archive 283 genomes corresponding to 152 fungal and Oomycete species as well as 201 genomes that correspond to seven bacteria, 39 plants and 105 animals. In addition, the number of tools in Favorite increased to 27. The Taxonomy Browser of CFGP 2.0 allows users to interactively navigate through a large number of genomes according to their taxonomic positions. The user interface of BLASTMatrix was also improved to facilitate subsequent analyses of retrieved data. A newly developed genome browser, Seoul National University Genome Browser (SNUGB), was integrated into CFGP 2.0 to support graphical presentation of diverse genomic contexts. Based on the standardized genome warehouse of CFGP 2.0, several systematic platforms designed to support studies on selected gene families have been developed. Most of them are connected through Favorite to allow of sharing data across the platforms.

## INTRODUCTION

Fungal genome sequencing has rapidly increased since the release of the genome sequences of *Saccharomyces cerevisiae* in 1996 (1). With the current and anticipated advances in sequencing technology (2,3), the rate of fungal genome sequencing will continue to accelerate. Currently, there exist more than 300 fully sequenced fungal genomes in the public domain (4,5), with many species and several isolates of previously sequenced species being sequenced (6,7). In addition, the 1000 Fungal Genome project (F1000; <http://1000.fungalgenomes.org/>) will greatly help us to uncover genomic underpinnings of fungal evolution and life styles via large-scale comparative genomics studies. In combination with genomes from plants and animals as well as fungi, in-depth comparative genomics across multiple eukaryotic kingdoms will be facilitated (8–10). To efficiently support such large-scale, genome-based inquiries, it is critical to archive the available genome sequences and annotation information in a standardized format so that they can be easily and efficiently retrieved and analyzed.

To address this need, in 2007, the first version of Comparative Fungal Genomics Platform (CFGP) was released with 65 fungal and Oomycete genomes (11). The CFGP was founded on a new user interface (UI) called Data-driven User Interface (DUI), which made use of its bioinformatics tools and the management of task histories easy and efficient. Since then, the number of genomes archived and bioinformatics tools have grown substantially. (Supplementary Table S1 and Table 1) Furthermore, the standardized genome data warehouse of CFGP has supported the development of multiple platforms that are specialized for supporting the archiving and

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**Table 1.** List of bioinformatics tools available in CFGP 2.0

Category	Name	Input data	References
Sequence search	BLAST	Sequences	(12)
	BLAST2	Sequences	(12)
	BLASTMatrix	Sequences	(11)
ID of functional domains	InterPro Scan	Sequences	(13)
Phylogenetic analysis	ClustalW	Sequences	(14)
	DNAML	Alignment	(15)
	PROML	Alignment	(15)
	DNAPARS	Alignment	(15)
	PROTPARS	Alignment	(15)
	PHYML	Alignment	(16)
ID of secreted proteins	SignalP 3.0	Sequences	(17)
	SigCleave	Sequences	(18)
	SigPred	Sequences	(19)
	RPSP	Sequences	(20)
	SecretomeP	Sequences	(21)
Subcellular localization	PSortII	Sequences	(22)
	predictNLS	Sequences	(23)
	ChloroP	Sequences	(24)
	TargetP	Sequences	(25)
Prediction of trans-membrane helices	TMHMM2	Sequences	(26)
Prediction of RNA secondary structure	tRNAscan-SE	Sequences	(27)
	mFold 3.2	Sequences	(28)
Post-translational modification	NetCGlyc	Sequences	(29)
	NetNGlyc	Sequences	—
	NetOGlyc	Sequences	(30)
	NetPhos	Sequences	(31)
Conserved motif search	MEME	Sequences	(32)

A total of 27 tools in nine categories are available via the Favorite browser of CFGP 2.0.

analysis of specific gene families and functional groups (Table 2). Some of these platforms share the Favorite of CFGP to provide an efficient mechanism for sharing data with CFGP and to enable the use of its bioinformatics tools for a variety of analyses. In this article, we outline the improvements made in CFGP 2.0 and how its standardized genome warehouse has been exploited in development of other comparative genomics platforms.

## METHODS

### System design

The structure and core databases of CFGP 2.0 are basically identical to those used for the first version. The system consists of databases including a standardized genome warehouse, wrapper programs written by the Perl and C languages and DUI. To balance the server load so as to ensure a more efficient operation of the system, its core databases were distributed in multiple servers, and more web servers were added. The MySQL relational database management system was used to manage and curate the data. Its web interfaces were written in PHP with javascript, and analysis functions in Favorite Browser

**Table 2.** List of online platforms and tools supporting studies on specific gene families or functional groups<sup>a</sup>

Name	URL	Reference
Cyber-infrastructure for <i>Fusarium</i>	http://www.fusariumdb.org/	(33)
Fungal Transcription Factor Database	http://ftfd.snu.ac.kr/	(34)
Fungal Cytochrome P450 Database	http://p450.riceblast.snu.ac.kr/	(35)
Seoul National University Genome Browser	http://genomebrowser.snu.ac.kr/	(36)
The Systematic Platform for Identifying Mutated Proteins	http://pimp.starfl.info/	(37)
Insect Mitochondrial Genome Database	http://www.imgd.org/	(38)
Fungal Secretome Database	http://fsd.snu.ac.kr/	(39)
Eukaryotic DNAJ/K Database	http://edd.snu.ac.kr/	—
Cell Wall-degrading Enzyme Database	http://www.cwde.org/	—

<sup>a</sup>These platforms were developed using the standardized genome warehouse and the web template engine of CFGP 2.0.

were relayed by Perl scripts and automatically coordinated by the system monitoring servers.

### Mining orthologs

The source code of InParanoid 4.1 was used for the identification of orthologs in the archived proteomes. First, the genomes of 35 species that are frequently utilized were subjected to ortholog identification (Supplementary Table S1). All pairwise comparisons of data from these 35 species were carried out. The latest version of InParanoid 7 provides orthologs from 100 eukaryotic genomes. However, some genomes that we have used were not included in the latest version; data for those species were downloaded from CFGP 2.0 and subsequently subjected to ortholog identification.

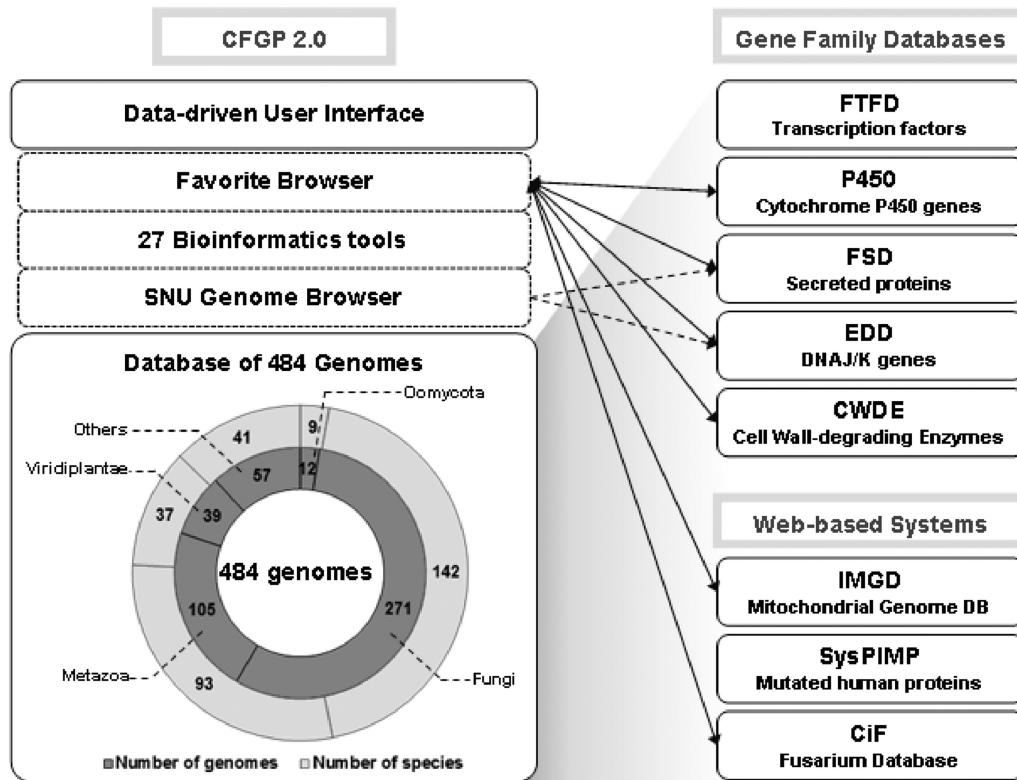
## EXPANDED GENOME DATA WAREHOUSE

The standardized genome warehouse of CFGP has been substantially expanded in both the number of species and taxonomic coverage. In addition to 283 genomes corresponding to 152 fungal and Oomycete species, 39 plant and 105 animal genomes have also been archived (Figure 1 and Supplementary Table S2). The animal and plant genomes were incorporated to enable comparative evolutionary genomics studies across multiple eukaryotic kingdoms.

## ENHANCED UTILITY AND NEW FEATURES

### Improved UI

The UI of CFGP 2.0 was greatly improved to provide better user experience. All modifications followed the HTML5 and CSS3 standards, on which most widely used web browsers are based. Three main application/utility



**Figure 1.** A diagram illustrating the system architecture and the content of the genomes archived in CFGP 2.0. Key features of CFGP 2.0 were depicted on the left. The web-based platforms that have been developed based on the standardized genome warehouse of CFGP 2.0 are listed on the right. Bidirectional arrows indicate that they support the Favorite Browser, which synchronizes with CFGP 2.0. Dashed arrows denote that SNUGB was integrated in two platforms, FSD and EDD. In the pie graph, the inner and outer circles represent the number of genomes and species for each taxon, respectively.

**CFGP Comparative Fungal Genomics Platform**

283 genomes from 152 fungal species | amethyst(jaeyoung Choi) is logged in. | Modify MyInfo | Logout | Withdrawal

SEQUENCE HISTORIES DOMAINS ANALYSIS FAVORITE SNUGB

**Favorite frame**

Search New

122 favorites. 144 Page 16 of 82 >|<

- 12377 1 objects | Updated @ Jan 16, 2012
- Saccharo10 0 objects | Updated @ Jan 10, 2012
- Zygo15 4 objects | Updated @ Jan 10, 2012
- Pezzo17 4 objects | Updated @ Jan 10, 2012
- Zygo14 0 objects | Updated @ Jan 10, 2012
- BZ02 6 objects | Updated @ Jan 10, 2012
- Saccharo9 6 objects | Updated @ Jan 10, 2012
- Saccharo99 0 objects | Updated @ Jan 10, 2012
- Saccharo100 0 objects | Updated @ Jan 10, 2012
- Scharedo7 5 objects | Updated @ Jan 10, 2012
- Verticillium1 0 objects | Updated @ Jan 10, 2012
- Basidiol02 4 objects | Updated @ Jan 10, 2012
- Fusarium08 4 objects | Updated @ Jan 10, 2012
- Fusarium07 6 objects | Updated @ Jan 10, 2012
- Fusarium06 4 objects | Updated @ Jan 10, 2012
- Fusarium05 5 objects | Updated @ Jan 10, 2012

**Presentation frame**

Magnaporthe oryzae 8 supercontig8. (Total Length : 4,490,059bp)

Range Option << < Start 333,678 bp End 354,544 bp >> >> Refresh

Viewing Option Contig Region Squish Transcript Pack View ORF Option Display View Exon/Intron Option Display Refresh

**Frame toggle buttons**

**Application frame**

Contig Browser List of proteins

Dataset Name : Magnaporthe oryzae 8

Chk	Locus name	Gene	Protein name	Length(aa)	Contig	Ch#	Function
<input checked="" type="checkbox"/>	MGG_0114670	acetylxylylan esterase	229	5	0		SNUGB
<input type="checkbox"/>	MGG_0984070	acetylxylylan esterase 2	299	6	0		SNUGB

There are 2 proteins in total.

Search by Protein name | acetylxylylan esterase | Search | View All | 10 Items per page

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Last Update : 2012-07-20 13:27:56 Total Access : 45,930 This site is compatible to at 1024x768.

**Figure 2.** Outline of the improved DUI of CFGP 2.0. The frames outlined in blue, orange and purple correspond to the Favorite, presentation and application frame, respectively. The buttons boxed in red are to hide or show Favorite and presentation frames, respectively.

frames were rearranged to make the switch from one frame to another more intuitive. The Favorite and presentation frames can be toggled for more flexible browsing (Figure 2). All web pages have been thoroughly tested with multiple web browsers, including Chrome, Firefox, Internet Explorer and Safari.

### Taxonomy browser

As the number of species representing diverse taxa continues to increase, a browsing tool based on simple text search (e.g. species name) was not sufficient to help users to efficiently explore available genomes. The Taxonomy Browser implemented in CFGP 2.0 provides predictive text feature as well as a hierarchical tree-based taxon

structure to show the taxonomic position of a chosen species. Once a specific species is selected, the number of genomes and available sequence types are listed with direct links to corresponding sequences.

### Seoul National University Genome Browser

The first version of CFGP did not offer a graphical interface to present the genomic context and notable features such as GC content, functional domains and the signal peptide. This new genome browser implemented in CFGP 2.0 enabled users to view such information in the chosen region. The target region of viewing can be selected by assigning the start and end positions with a mouse or by typing in its genome coordinate (Figure 3).



**Figure 3.** A screenshot of SNUGB implemented in CFGP 2.0. SNUGB allows users to view 13 biological features and the gene structures in the selected genome region. Those features include GC contents, functional domains, nuclear localization signals, signal peptides and trans-membrane helices.

## New bioinformatics tools added to the Favorite Browser

Compared with the first version that only provided six tools, CFGP 2.0 is equipped with 27 tools covering nine categories of data analysis or viewing (Table 1). This addition enables users to perform more analyses without leaving CFGP.

### Ortholog browsing function

Finding orthologs for a specific gene in multiple species often requires numerous BLAST searches and validation processes. In the first version of CFGP, we tried to eliminate copy-and-paste of sequences by incorporating the DUI (11). In CFGP 2.0 we simplified the identification and collection of orthologs by offering pre-computed data. There are several ortholog identification programs such as InParanoid (40), Ortholog, MSOAR (41) and THOR (42). We adopted InParanoid to identify orthologs via pairwise comparisons among 35 frequently accessed genomes. For every protein sequence encoded by each of these 35 genomes, orthologous genes in the other 34 genomes are provided to allow a quick overview of its distribution among these species and also to support their further analyses by saving them into a Favorite on the fly.

## FUNCTIONAL/EVOLUTIONARY GENOMICS PLATFORMS DEVELOPED BASED ON THE STANDARDIZED GENOME WAREHOUSE OF CFGP 2.0

Via the use of the standardized genome warehouse of CFGP 2.0, a number of platforms that aim to support comparative analyses of specific gene families and/or functional groups have been developed: (i) Cyber-infrastructure for *Fusarium* (CiF; <http://www.fusariumdb.org/>) (33), (ii) Fungal Transcription Factor Database (FTFD; <http://ftfd.snu.ac.kr/>) (34), (iii) Fungal Cytochrome P450 Database (FCPD; <http://p450.riceblast.snu.ac.kr/>) (35), (iv) Fungal Secretome Database (FSD; <http://fsd.snu.ac.kr/>) (39), (v) Eukaryotic DNAJ and DNAK Database (EDD; <http://edd.snu.ac.kr/>) (Cheong *et al.*, manuscript in preparation) and (vi) Cell Wall-degrading Enzymes Database (CWDE; <http://www.cwde.org/>) (Choi *et al.*, manuscript in preparation). The Seoul National University Genome Browser (SNUGB) (<http://genomebrowser.snu.ac.kr/>) (36) was also implemented in FSD and EDD. The Insect Mitochondrial Genome Database (IMGD; <http://www.imgd.org/>) (38) employs the Species-driven UI, which enables intuitive and fast taxonomical browsing with multiple add-on analysis functions. Finally, the Systematic Platform for Identifying Mutated Proteins (SysPIMP; <http://pimp.starfl.info/>) (37) was developed to support the identification of mutations related to human diseases. The Favorite Browser of CFGP 2.0 is connected with many of those platforms to efficiently support data exchange and sharing across multiple platforms. All the data saved in the Favorite Browser are synchronized in real-time so that users can fully exploit data and functions provided by these platforms.

## FUTURE DIRECTIONS

To keep up with the rapidly released and updated eukaryotic genomes, CFGP 2.0 will be updated on a regular basis. We will integrate more useful modules, software or interface scheme to continuously improve the environment for users conducting comparative and evolutionary genomics studies. In order to support efforts to uncover possible functions of many hypothetical genes, the ortholog information database will be expanded by adding the corresponding information from more species.

## SUPPLEMENTARY DATA

Supplementary Data are available at NAR Online: Supplementary Tables 1 and 2.

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